

**U.S. High Production Volume (HPV)
Chemical Challenge Program**

**CATEGORY DEVELOPMENT AND JUSTIFICATION,
AND COMPLETED TEST PLAN FOR COBALT STEARATE
AND FATTY ACIDS, TALL OIL, COBALT SALTS**

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Prepared by

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on behalf of

The Metal Carboxylates Coalition

A SOCMA Affiliated Consortium

Specifically Sponsored By

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SUMMARY

The Metal Carboxylates Coalition has sponsored 20 compounds that are metal salts of carboxylic acids (metal carboxylates). These compounds readily dissociate to the corresponding metal and carboxylic acid. The HPV endpoints are fulfilled using a combination of data from the parent molecule, as well as for the dissociation products; that is, a metal salt and/or a carboxylic acid. Selected testing of the parent molecules has been proposed to further fulfill HPV endpoints. Robust summaries are provided for the parent molecules as well as the dissociation products.

This submittal provides the information for:

Cobalt Stearate

CASRN 13586-84-0

Fatty acids, Tall Oil, Cobalt Salts

CASRN 61789-52-4

The proposed testing is presented in the attached Test Plan matrix (Table 6)

1.0 BACKGROUND

This submittal provides the information for:

Cobalt Stearate

CASRN 13586-84-0

Fatty Acids, Tall Oil, Cobalt Salts

CASRN 61789-52-4

Co stearate is the cobalt salt of stearic acid. Because cobalt is divalent, two stearic acid molecules are involved. The structural formula is $\text{Co}(\text{C}_{18}\text{H}_{35}\text{O}_2)_2$. The Co salts of fatty acids, tall oil are more difficult to characterize chemically because the tall oil fatty acids are derived from the fractional distillation of crude tall oil, which is a by-product from the pulping of pine trees. The mixture of fatty acids in pine trees varies by species and even within species (Pine Chemicals Association, 2004). The composition of a typical tall oil fatty acid includes oleic acid (48%), linoleic acid (35%), conjugated linoleic acid (7%), stearic acid (2%), palmitic acid (1%), and other acids and unsaponifiable matter (Pine Chemicals Association, 2004). Oleic acid and linoleic acid, like stearic acid, are C18 fatty acids with slightly differing degrees of saturation.

Co stearate and fatty acids, tall oil, Co salts are high molecular weight compounds. The molecular weight for Co stearate is 625.9. The molecular weight of fatty acids, tall oil, Co salt is undefined due to the undefined nature of the acid component; however, the typical composition would be largely oleic and linoleic acid, both of which are C18 unbranched aliphatic acids, as is stearic acid. Thus the molecular weight of fatty acids, tall oil, Co salts would be similar to that of Co stearate.

Figure 1 provides the structure of Co stearate. Figure 2 provides the structures of oleic acid and linoleic acid, major components of fatty acids, tall oil. The Co salts of fatty acids, tall oil consist of Co associated with the various acid moieties, similar to Co stearate.

1.1 Use Patterns for Metal Carboxylates

The metal carboxylates function to deliver a metal ion into chemical reactions. The carboxylic acids (acids) are tailored for use in different products or chemical reactions.

In general the Co carboxylates are used as oxidative polymerization catalysts in many product areas. These areas include, but are not limited to: ink and paint driers; unsaturated polyester resins, and hydrodesulfurization in their manufacturing; and the making of the insecticide DEET (diethyltoluamide). Some of these carboxylate compounds are used in oxygen scavenger plastics as well (for example, plastic bottles). The tire industry also uses Co carboxylate compounds as adhesion promoters in tire manufacturing. These compounds facilitate adhesion between the rubber in the steel cords. The metal (not salt) loadings range from 0.01 – 0.5% depending upon the application.

1.2 Common Characteristics of Metal Carboxylates

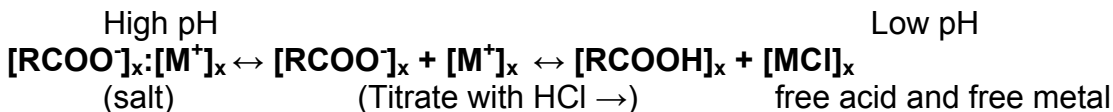
These two metal carboxylates (Co stearate and fatty acids, tall oil, Co salts) are functionally similar and have the same ionizable substituents, the same metal cation, and a structurally similar carboxylic acid group (RCOOH). These compounds are divalent compounds and have two carboxylic acid moieties per molecule. The metal carboxylate salts are designed to add metals to chemical reactions; therefore, they are designed to readily dissociate into the free metal and free acid.

2.0 Dissociation Studies

One key characteristic of metal carboxylates is that they readily dissociate from an ion pair into free metal and free acid. They are found as partially dissociated products in the ambient environment (i.e., neutral pH). Dissociation is a reversible process and the proportion of dissociated salt present is dependent on the pH and pKa (the dissociation constant), which is the pH at which 50% dissociation occurs. In the low pH environment of the digestive tract (e.g., pH 1.2) complete dissociation will occur for these metal carboxylates. The transport and bioavailability of the metals and acids are determined by their solubility in environmental media and biological fluids which is determined by environmental parameters such as pH.

The Metal Carboxylates Coalition conducted studies to determine the dissociation constants of each of these compounds. The mean pKa value for Co stearate was 7.5 at 20°C while the mean pKa value for fatty acids, tall oil, Co salts was 5.82. These results indicate that significant dissociation will occur at approximately neutral pH (i.e., representative of aquatic and marine ecosystems), while complete dissociation will occur at physiologically relevant pH of the mammalian stomach (pH 1.2). These findings are particularly important in relating available data for the respective acids and metals to support the existing data for Co stearate and fatty acids, tall oil, Co salts in the fulfillment of critical endpoints.

Dissociation is a reversible reaction, splitting the parent compound into two or more chemical species which may be ionic, but are not necessarily so. The process can be generally represented as:



The pKa and pH are equal when the metal carboxylate salt is 50% dissociated. The parent compounds, the metal carboxylate salts, are associated ionized molecules.

The dissociation constant is important for two reasons. First, it determines the proportion of any specific acid or metal that is dissociated at a given pH. The free acid and corresponding free metal are often much different than the salt (ion pair) moiety in characteristics such as solubility, adsorption, and toxicity. The proportion of dissociation influences the behavior of the substance in the environment and bioavailability of the acid and metal constituents of metal carboxylate salts.

The dissociation constants for 18 related metal carboxylate compounds tested have pKa (pKb) values (pKa1) in the neutral range (5.088 to 8.448). This indicates that in the neutral pH range, significant portions of the metal carboxylates will be dissociated. In addition, at the low pH of the mammalian stomach (pH 1.2) all of the metal carboxylates would be expected to be completely or nearly completely dissociated. This indicates that the absorption and any observed toxicity would be independent for the respective acid and metal when administered orally.

The dissociation constants show that at the pH of the stomach and at the pH of environmental media, the important moieties are the ionized free acid and metal. Because of this, environmental fate, ecotoxicity, and mammalian toxicity of the free acid, or that for a simple salt which would readily dissociate (e.g., the sodium salt), can serve as surrogate data for the acid component of respective metal carboxylates. Similarly, under these conditions, data for the metal ion can be represented by fate and toxicity data on free metal ion or simple metal salts (e.g., metal chlorides). Therefore, the role in any observed toxicity for acids and metals can be evaluated independently (i.e., as the free metal and/or free acid).

3.0 Bioequivalency

The work described below by Stopford et al. (2003)¹ shows that Co chloride is similar to, or more bioavailable than, the corresponding Co carboxylate salts, which makes the chloride a conservative surrogate in estimating bioavailability and toxicity of dissociated metal. Co chloride has thus been emphasized during preparation of the attached robust summaries and provides the preferred surrogate data for Co carboxylate salts.

The recent studies by Stopford et al. to evaluate the “bioequivalency” (an estimate of bioavailability) of Co compounds included three Co carboxylates and Co chloride. The solubility of these compounds in synthetic biological fluids

1

Stopford, W., J. Turner, D. Cappellini, and T. Brock (2003). “Bioaccessibility Testing of Cobalt Compounds.” J. Environ Monit., 5:675-680.
C.

(gastric juices, intestinal juices, several interstitial fluids, and cytosol) showed that these salts were completely dissociated and dissolved at gastric pH and cytosolic pH. The dissolution of these compounds ranged from 26.1% to 80.4 % of available Co at neutral pH (Table 1). The results for Co chloride and Co 2-ethyl-hexanoate were very similar at acidic and neutral pH. Co neodecanoate and Co naphthenate showed similar levels of dissolution at acidic (gastric and cytosolic) pH, but smaller proportions of the metal component of these compounds were dissolved at neutral pH. The differences in dissolution for these metal carboxylates at neutral pH in synthetic body fluids could be related to differences in their dissociation constants.

These data are valuable in understanding Co stearate and fatty acid, tall oil, Co salts for three reasons:

1. They confirm the prediction that these compounds would be expected to be completely dissociated in the gastrointestinal tract (low pH) and a substantial proportion would be expected to be dissociated and bioavailable at neutral pH (7.4).
2. The fraction of the three Co carboxylates evaluated by Stopford et al. that was dissolved at acidic and neutral pH was very similar for different acid constituents with a range of molecular weights and chain lengths. This finding greatly strengthens the extrapolation of the results to Co stearate and fatty acids, tall oil, Co salts.
3. The work by Stopford et al. shows that Co chloride is similar to, or more bioavailable than, the corresponding Co carboxylate salts, which makes the chloride a conservative surrogate in estimating bioavailability and toxicity of dissociated metals. Co chloride has been emphasized during preparation of the attached robust summaries and provides the preferred surrogate data for the Co carboxylate salts.

Work by Firriolo² demonstrated that absorption, distribution, and excretion of Co from cobalt carboxylic acids are independent of the acid. This work was based on Co chloride and Co naphthenate and confirms observations by Stopford et al. that dissociation of the carboxylate is complete at the pH of the stomach.

² Firriolo, J.M. 1992. Disposition and toxicity after oral and intravenous administration of Co naphthenate and Co chloride in rats. Ph.D. Dissertation, University of Arizona.

4.0 Supporting Data for HPV Chemicals and their Dissociation Products

Data for Co stearate (Appendix A) and fatty acids, tall oil, Co salts (Appendix B) and their dissociation products (Co chloride, stearic acid, and fatty acids, tall oil [Appendixes C, D, and E, respectively]) are provided in robust summary format.

Consistent with discussions between the Metal Carboxylates Coalition and the EPA, data for the dissociation products (metals and acids) are recognized as being essential to understanding the environmental fate and toxicological characteristics of the respective metal carboxylate salts. Data for stearic acid, fatty acids, tall oil, and Co are useful in characterizing the hazard of the Co stearate and fatty acids, tall oil, Co salts.

In summary, the key points relative to these two HPV chemicals are:

- Dissociation to the carboxylic acids and Co (described as Co chloride);
- Dissociation constants (pKa) in the circum neutral range (5.82 to 7.5);
- Complete or nearly complete dissociation at gastric and cytosolic pH levels;
- A moderate to high proportion of dissociation in the neutral pH range;
- General bioequivalency for salts with the same metal cation (e.g., Co) and different acids or the chloride salt;
- Co carboxylates have the same use pattern, to provide free metal ion to chemical reactions.
- Existing data for the parent molecule or both of its dissociation products will be sufficient to address specific endpoints.

5.0 Proposed Test Plan

The Metal Carboxylates Coalition has relied on the fact that these compounds will dissociate and that the respective acid (stearic acid or fatty acids, tall oil), and metal (Co) are the chemicals of interest. Studies conducted by the Metals Carboxylates Coalition have demonstrated that dissociation of these materials will occur readily in water at neutral pH's and completely at the pH of the stomach (pH 1.2). This is consistent with data for other metal carboxylates.

The Metal Carboxylates Coalition is relying on the data for Co and for stearic acid to support Co stearate and to minimize unnecessary testing. A robust summary document has been prepared for Co chloride, which describes the necessary endpoint data under the HPV Program (Appendix C). A robust summary document has also been prepared for stearic acid (Appendix D). Stearic acid has a long history of safe use in foods and cosmetics. This compound is sponsored within the Aliphatic Acids Category under the HPV Challenge

Program. More complete or more robust data may become available following the Aliphatic Acids Category submission to the EPA by The Soap and Detergent Association.

To support fatty acids, tall oil, Co salts, the Metal Carboxylates Coalition is relying on the data for Co and for fatty acids, tall oil and Co stearate. As mentioned previously, the robust summary document prepared for Co chloride is attached as Appendix C. Fatty acids, tall oil are sponsored by the Pine Chemicals Association, Inc. as part of the category Tall Oil Fatty Acids and Related Substances. The robust summaries for fatty acids, tall oil submitted to EPA as part of the final submission from the Pine Chemicals Association, dated August 2004, are included as Appendix E. Also included in Appendix E is the IUCLID dataset for fatty acids, tall oil, dated February 2000.

Tables 2 - 5 provide a summary of the data for Co stearate and fatty acids, tall oil, Co salts, as well as their dissociation products

Physicochemical Properties

The physicochemical properties are summarized in Table 2. The Metal Carboxylates Coalition conducted GLP studies to determine several properties of Co stearate and fatty acids, tall oil, Co salts, including melting point, boiling point, water solubility and dissociation constant. Melting point studies were performed to generate data for both HPV compounds (see Table 2). In studies conducted to determine the boiling points, Co stearate decomposed before boiling could occur and a boiling point was not observed for fatty acids, tall oil, Co salts. Based upon the properties of the respective acids, the vapor pressure of the two HPV compounds is expected to be low. Studies indicated the water solubility of the two compounds was fairly low, but greater than their respective acids. This result may be related to the procedure used, which quantified the amount of test compound in solution by measuring the amount of Co. Since Co stearate and fatty acids, tall oil, Co salts dissociate, the water solubility test results may reflect dissociation rather than solubility per se. The octanol-water partition coefficient (Kow) is a property that is determined on unionized, undissociated chemicals and therefore is not an appropriate property to measure for metal carboxylates. The Kow of the respective acids provides surrogate data to estimate this property for the dissociated Co stearate and fatty acids, tall oil, Co salts.

No additional physical chemical properties testing was proposed.

Environmental Fate

Table 3 provides a summary of the available environmental fate data for the two HPV chemicals, as well as their dissociation products. The Metal Carboxylates Coalition conducted studies to determine the dissociation constants of Co stearate and fatty acids, tall oil, Co salts; the resulting pKa values were 7.50 and 5.82, respectively. These results indicate that the environmental fate characteristics of these chemicals will be dependent upon the characteristics of their dissociation products, data for which are presented in Table 3. The dissociated Co metal will not photodegrade or biodegrade. The respective acids, however, are amenable to these degradation processes. Predictions based upon structure-activity models (e.g., EPIWIN) indicate that stearic acid is photodegradable and would tend to be found in the sediment or soil compartments of the environment. Several laboratory studies indicate that both stearic acid and fatty acids, tall oil are reported to be readily biodegradable. Predictions for photodegradation and transport (fugacity) have been calculated using EPIWIN for oleic acid and linoleic acid, the two major components of a typical fatty acid, tall oil. These results are similar to those for stearic acid.

A biodegradation study with Co stearate was proposed and conducted. Biodegradation data will show that the rate of degradation for the Co stearate salt is the same as stearate alone and that the Co does not inhibit biodegradation of the stearate. Both Co stearate and fatty acids, tall oil, Co salts would have the same combined effect on biodegradation; therefore only one study with Co stearate was conducted. Fatty acid tall oil Co salts are filled by both read across from Co stearate and by data for the acid dissociation product (Table 6). It is assumed that since the Co stearate salt was "not readily biodegradable" the Fatty acid tall oil Co salts would also be "not readily biodegradable."

Environmental Effects

Table 4 provides a summary of the available environmental effects data for Co stearate, and fatty acids, tall oil, Co salts, as well as their dissociation products. No information is available for the two HPV chemicals. For the dissociation products, adequate data exist to characterize the aquatic toxicity of Co. Studies have been conducted to determine the acute toxicity of fatty acids, tall oil to fish, invertebrates and algae, providing sufficient information for these endpoints. However, for stearic acid, only data on toxicity to fish are available, and this is for a study of time to lethality (LT50 endpoint), so it is marginally useful. It is anticipated that additional aquatic toxicity data for stearic acid will be generated by the Aliphatic Acids Consortium. To demonstrate that dissociation product data is representative of the aquatic toxicity for the two HPV chemicals, it is proposed that acute toxicity studies for fish, daphnia and algae be conducted with Co stearate.

Acute toxicity studies with fish, daphnia and algae were conducted to characterize the aquatic toxicity of Co stearate. In addition, an acute daphnia study with fatty acids, tall oil, Co salts was conducted as a bridging study to demonstrate that the dissociation product data are representative for this metal carboxylate salt. The results of >4.1 for Co stearate and 8.0 for Fatty acid tall oil Co salts shows that these are similar and serve to bridge to all three environmental effects endpoints with read across to fish and algae.. The acid alone was much less toxic indicating that Co plays a key role in observed level of toxicity of these Co carboxylates to aquatic species.

Human Health Effects

Data elements for human health effects endpoints were examined for Co stearate and fatty acids, tall oil, Co salts, and their dissociation products (Table 5). Mammalian acute toxicity studies were conducted with both Co stearate and with fatty acids, tall oil, Co salts (e.g., Acute Oral LD50) and compared as bridging study and to compare to dissociation products. For Co chloride, several studies are available to document acute oral toxicity and repeated dose toxicity. Male reproductive effects have been demonstrated in rats and mice and developmental toxicity studies exist for both rats and mice. Co (II) is generally not mutagenic in bacterial assays but has genotoxic effects in mammalian systems. For fatty acids, tall oil, data are available for acute oral toxicity, repeated dose toxicity, and reproductive/developmental toxicity. In addition, tests have demonstrated that fatty acids, tall oil was not mutagenic in bacterial assays but was clastogenic to mammalian cells (though at cytotoxic concentrations).

An oral LD50 study was conducted for Co stearate and fatty acids, tall oil, Co salts as part of establishing the category approach, i.e., that the dissociation products can be used to predict the toxicity of the salts. It is clear from the data in Table 5 that Co is the toxicant of concern in acute mammalian toxicity. Co LD50 values are approximately 1/10 of the relative salt toxicities (i.e., 190 versus 2000 mg/kg) which are equivalent when the Co stearate and fatty acid tall oil Co salts are normalized for 9.46% and 9.49% Co content, respectively. The acid LD50s are two to five fold higher than the salts. The results were very similar for both salts indicating that the mammalian acute studies are determined by Co content and that higher tiered mammalian studies would also yield similar results with Co being the dominant toxicant of concern.

An OECD 422 study with Co stearate was conducted as a bridging study to show that dissociation product data is representative of the mammalian toxicity for these two metal carboxylate salts. When the results of the OECD 422 study with Co stearate (NOEL 5.0) is normalized for 9.46% Co. It is similar to the 0.6 mg/kg/day NOAEL reported for CoCl₂, for repeated dose; below the effects level reported for rat reproduction studies and developmental studies indicating that the Co concentration is the key indicator of toxicity in these higher tiered studies.

Since fatty acid tall oil Co salts has essentially the same proportion of Co and has highly similar acid moieties (see fig. 2) the repeated dose, reproduction and developmental endpoints are filled by read across from Co stearate and the dissociation products specifically Co as CoCl_2 (See Tables 5 and 6).

There were no in vitro bacterial assays with the two Co carboxylates, but the data element is filled with data for the dissociation products. All Dissociation products including Co were negative for bacterial assays. Because there were no data available on the genetic toxicity of stearic acid to mammalian systems, a chromosomal aberration study was conducted for Co stearate. A chromosomal aberration study was also conducted for fatty acids, tall oil, Co salts based on reported clastogenicity of both dissociation products (Co and fatty acids, tall oil) (See Table 6). Both compounds were positive in Chinese hamster ovary cell chromosomal aberration studies (See Table 5).

5.1 TEST PLAN SUMMARY

Table 6 summarizes the test plan for Co stearate and fatty acids, tall oil, Co salts. All studies are complete and all endpoints are filled. No additional studies are needed.

FIGURES

Figure 1: Cobalt Stearate

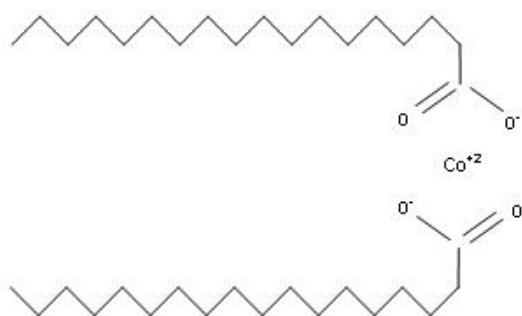
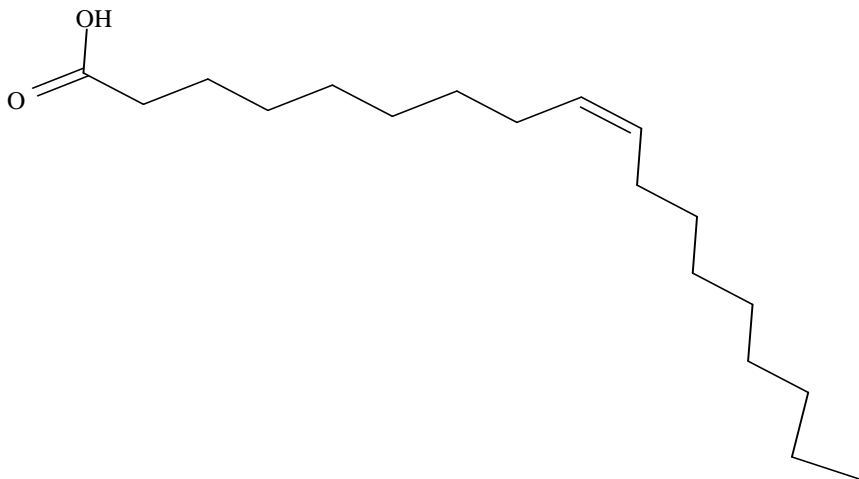


Figure 2: Fatty acids, tall oil: typical major components

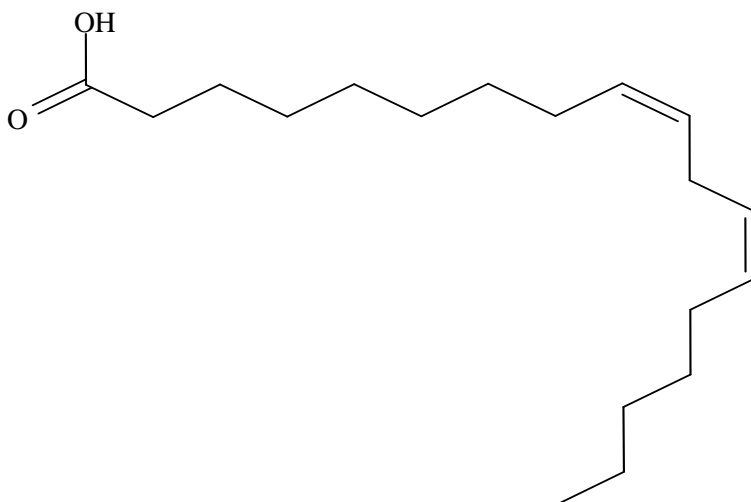
Oleic acid

$C_{18}H_{34}O_2$



Linoleic acid

$C_{18}H_{32}O_2$



TABLES

Table 1. Results of Extraction of Cobalt from Surrogate Biological Fluids

Matrix (pH)	Maximum Solubility (% of available metal)			
	CoCl ₂	Co 2-ethyl-hexanoate	Co naphthenate	Co neodecanoate
Gastric pH (1.5)	>91.6	100	>85.7	100
Intestinal pH (7.4)	>79.4	50.8*	45.4*	30.8*
Alveolar pH (7.4)	>68	>59.6	35.4*	26.1*
Interstitial pH (7.4)	78.4	>80.4	40*	43.1*
Serum	>85	>66.9	42.9*	46.6*
Intracellular pH (4.5)	>89.6	100	>79.1	>78.1

* maximum extraction level at 72 hours

All data is taken from Stopford et al. (unpublished) Bioequivalency Testing of Cobalt Compounds. Conducted by Duke University Medical Center, Division of Occupational and Environmental Medicine for the Cobalt Development Institute.

Table 2. Summary of Available and Relevant Physical/Chemical Properties Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Physical/Chemical Properties				
	Melting Point (deg C)	Boiling Point (deg C)	Vapor Pressure (hPa)	Partition coefficient (log Kow)	Water Solubility (mg/L)
<i>Dissociation Product:</i> Cobalt chloride	735	1,049	NA	NA	450,000
Cobalt stearate	45.1 – 79.3	ND	-	NA	6.4 @ 20°C
<i>Dissociation Product:</i> Stearic acid	69 - 70	383	1.33 @173.7	8.42	0.568 @ 25°C
Fatty acids, tall oil, cobalt salts	-38 to -39	ND	-	NA	149 @ 20°C
<i>Dissociation Product:</i> Fatty acids, tall oil	NA	160 - 210 @ 6.6 hPa	negligible	4.4 – 8.3 @ pH 2; 3.6 – 7.4 @ pH 7.5	12.6

ND = no data; testing did not yield results for boiling point

NA = not applicable due to substance properties

Table 3: Summary of Available and Relevant Environmental Fate Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Environmental Fate			
	Stability in Water	Photo-degradation	Level III Fugacity Model	Biodegradation
<i>Dissociation Product:</i> Cobalt chloride	(high water solubility)	NA	NA	NA
Cobalt stearate	Dissociates: pKa = 7.50 @ 20°C	-	-	8.81% in 28 days (Not readily biodegradable)
<i>Dissociation Product:</i> Stearic acid	(low water solubility)	T ½ = 0.5 days	Air: 0.676 Water: 7.19 Soil: 28.9 Sediment: 63.3	Readily biodegradable
Fatty acids, tall oil, cobalt salts	Dissociates: pKa = 5.82 @ 20°C	-	-	-
<i>Dissociation Product:</i> Fatty acids, tall oil ⁽¹⁾	(low water solubility)	T ½ = 2 hours or less	Air: <0.1 Water: 7-8 Soil: 28-29 Sediment: 63-64	Readily biodegradable

NA = not applicable due to substance properties

⁽¹⁾ Photodegradation and fugacity results are averages of modeled results for oleic acid and linoleic acid, two components of fatty acids, tall oil

Table 4. Summary of Available and Relevant Environmental Effects Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Environmental Effects		
	Acute Toxicity to Fish (mg/L)	Acute Toxicity to Daphnia (mg/L)	Acute Toxicity to Algae (mg/L)
<i>Dissociation Product:</i> Cobalt chloride	1.41 – 333 (96-h LC50)	1.52 – 5.5 (48-h EC50)	0.52 (96-h EC50)
Cobalt stearate	-	>4.1 mg cobalt stearate/L (>0.38 mg Co/L)	-
<i>Dissociation Product:</i> Stearic acid	LT50 data (marginally useful)	-	-
Fatty acids, tall oil, cobalt salts	-	8.8 mg cobalt tallate/L (0.77 mg Co/L)	-
<i>Dissociation Product:</i> Fatty acids, tall oil	10 (96-h LC50) to > 1000 (96-h LL50)	55.7 (48-h EC50) to > 1000 (48-h LL50)	0.79 – 9 (EC50) to 854 (72-h EL50)

Table 5. Summary of Available and Relevant Human Health Effects Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Human Health Effects				
	Acute Toxicity (mg/kg)	Repeat Dose Toxicity	Reproductive Effects	Developmental Effects	Genetic Toxicity
<i>Dissociation product:</i> Cobalt chloride	LD50 = 42.4 – 190 (rat) LD50 = 89.3 (mouse)	NOAEL = 0.6 mg Co/kg; LOAELs 0.5 – 30.2 mg Co/kg/day	Effects in rats at 13.2 – 30.2 mg Co/kg/d; mice at 23-58.9 mg Co/kg/d	NOAEL = 24.8 mg/kg/d (mice); 81.7 mg Co/kg in screening study (mice)	Co (2+) generally non-mutagenic in bacterial assays; genotoxic/mutagenic/clastogenic in mammalian systems
Cobalt stearate	>2000 mg/kg/kg-	-See reproduction	NOEL = 5.0 mg/kg/day-	See reproduction -	Positive-
<i>Dissociation Product:</i> Stearic acid	LD50 = 4600 (rat) LD50 > 10,000 (rat)	50 g/kg/d for 24 weeks produced reversible lipogranulomas in rats; Severe effects in rats, including mortality, at 3000 ppm	-	-	Not mutagenic in bacterial assays
Fatty acids, tall oil, cobalt salts	2000 mg/kg	-	-	-	-Positive
<i>Dissociation Product:</i> Fatty acids, tall oil	LD50 > 10,000 (rat)	NOEL = 2500 mg/kg/d (rat 90-d, diet)	NOAEL = 5000 mg/kg/d (rat, 2 gen study)	NOAEL = 5000 mg/kg/d (rat, 2 gen study)	Not mutagenic in bacterial assays; clastogenic to mammalian cells but at cytotoxic concentrations

Table 6: Test Plan for Cobalt Stearate and Fatty Acids, Tall Oil, Cobalt Salts

Endpoint	Cobalt Stearate					Fatty Acids, Tall Oil, Cobalt Salts				
	Co stearate	Stearic acid	Co chloride	Data Used or New Data	OECD Guideline	FA, Tall Oil, Cobalt Salts	FA, Tall Oil	Co chloride	Data Used or New Data	OECD Guideline
<i>Physicochemical Properties</i>										
Melting point	Y	Y	Y	A		Y	NA	Y	A	
Boiling point	Y	Y	Y	A		Y	Y	Y	A	
Vapor pressure	N	Y	NA	DP		N	Y	NA	DP	
Partition coefficient	NA	Y	NA	NA		NA	Y	NA	NA	
Water Solubility	Y	Y	Y	A		Y	Y	Y	A	
<i>Environmental Fate</i>										
Photodegradation	N	Y	NA	DP		N	Y	NA	DP	
Stability in water	Y	Y	Y	A		Y	Y	Y	A	
Fugacity	N	Y	NA	DP		N	Y	NA	DP	
Biodegradation	Y	Y	NA	New	301	N	Y	NA	R/DP	
<i>Ecotoxicity</i>										
Acute Fish	Y	N	Y	New	203	N	Y	Y	R/DP	
Acute Daphnia	Y	N	Y	New	202	Y	Y	Y	New	202
Acute Algae	Y	N	Y	New	208	N	Y	Y	R/DP	
<i>Mammalian Toxicity</i>										
Acute	Y	Y	Y	New	425	Y	Y	Y	New	425
Repeated Dose	Y	Y	Y	New	422	N	Y	Y	R/DP	
Reproductive	Y	N	Y	New	422	N	Y	Y	R/DP	
Developmental	Y	N	Y	New	422	N	Y	Y	R/DP	
Genetic Toxicity (Bacteria)	N	Y	Y	DP		N	Y	Y	DP	
Genetic Toxicity (Mammalian)	Y	N	Y	New	473	Y	Y	Y	New	473

Y = Acceptable data available

N = No acceptable data available

NA = Not applicable due to physical/chemical properties of the substance

A = Endpoint requirement fulfilled with adequate existing data

New = Endpoint requirements to be fulfilled with new testing

DP = Endpoint requirements to be fulfilled using data for dissociation products

R = Use of category approach, e.g. that these two compounds are essentially the same and toxicity for one salt can be predicted from data for the other salt, when dissociation product data is available.

APPENDIX A
COBALT STEARATE ROBUST SUMMARIES

APPENDIX B

FATTY ACID, TALL OIL, COBALT SALTS ROBUST SUMMARIES

APPENDIX C
COBALT CHLORIDE ROBUST SUMMARIES

APPENDIX D
STEARIC ACID ROBUST SUMMARIES

APPENDIX E

FATTY ACIDS, TALL OIL ROBUST SUMMARIES